

What is claimed is:

- 1 1. A method for quantifying the osteoinductive potential of a collection of like
2 implant material intended for implantation into human or non-human recipients in need
3 thereof comprising:
4 (a) releasing osteogenic factors from a representative sampling of a collection of
5 like implant materials to produce an implant releasate containing said
6 osteogenic factors; and
7 (b) quantifying the concentration of at least one osteogenic factor present in said
8 implant releasate, wherein said quantifying occurs *in vitro* and does not
9 require implantation of said materials *in vivo* or use of complex biological
10 living materials; and
11 (c) determining a value of osteogenic potential for said representative sampling
12 by corresponding said concentration of at least one osteogenic factor with a
13 similar value on a predetermined curve;
14 whereby the osteogenic potential of said collection is realized. .
- 1 2. The method according to claim 1, wherein said implant material comprises bone.
- 1 3. The method according to claim 2, wherein said bone implant material comprises
2 autograft, allograft, xenograft, cortical bone, cancellous bone, and combinations thereof.
- 1 4. The method according to claim 3, wherein said releasing of step (a) comprises
2 demineralizing bone implant material to produce a substantially demineralized bone
3 implant matrix; optionally said demineralizing bone implant material comprises reducing
4 calcium concentration to about 2 percent or less.
- 1 5. The method according to claim 4, wherein said releasing further comprises
2 dissolving said demineralized bone implant matrix.

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1 6. The method according to claim 5, wherein said dissolving comprises contacting
2 said demineralized bone implant matrix with enzymes that do not destroy osteoinductive
3 factors present in said implant releasate, but which dissolve or otherwise dissociate said
4 demineralized bone matrix to produce a dissolved implant releasate.

1 7. The method according to claim 6, wherein said enzymes comprise collagenase.

1 8. The method according to claim 6, wherein said method further comprises
2 removing particulate debris from said dissolved implant releasate.

1 9. The method according to claim 8, wherein said removing comprises centrifuging
2 said dissolved implant releasate and retaining the centrifugation supernatant to provide an
3 implant releasate supernatant.

1 10. The method according to claim 9 further comprising removing low molecular
2 weight non-osteogenic factor molecules from said implant releasate supernatant.

1 11. The method according to claim 10, wherein said removing low molecular weight
2 non-osteogenic factor molecules comprises subjecting said implant releasate to dialyzing,
3 ultrafiltering, size-exclusion fractionating, precipitating, or combinations thereof.

1 12. The method according to claim 1, wherein said at least one osteogenic factor
2 comprises at least one mitogen and at least one morphogen .

1 13. The method according to claim 1, wherein said at least one osteoinductive factor
2 is selected from the group consisting of bone morphogenetic proteins, tissue growth
3 factors, fibroblast growth factors, platelet derived growth factors, vascular endothelial
4 growth factors, cartilage derived morphogenetic proteins, insulin-like growth factors, and
5 combinations thereof.

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1 14. The method according to claim 1, wherein said at least one osteogenic factor is
2 selected from the group consisting of transforming growth factors TGF- α , TGF- β , bone
3 morphogenic protein BMP-1, BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-7, BMP-8
4 and combinations thereof.

1 15. The method according to claim 14 wherein said at least one osteogenic factor
2 comprises TGF- β 1 plus BMP-2 or BMP-4 or both.

1 16. The method according to claim 1, wherein said quantifying comprises utilizing an
2 immunoassay which detects specific osteoinductive factors present in said implant
3 releasate.

1 17. The method according to claim 16, wherein said immunoassay is selected from
2 the group consisting of enzyme-linked immunosorbent assay (ELISA),
3 radioimmunoassay, immunoprecipitation or combinations thereof.

1 18. The method according to claim 16 wherein said quantifying comprises contacting
2 said at least one osteogenic factor with an antibody specific thereto under conditions to
3 allow for specific binding of said antibody to said at least one osteogenic factor to occur,
4 and measuring said specific binding of said antibody to said at least one osteogenic
5 factor.

1 19. The method according to claim 1, wherein said osteoinductive factors are
2 quantified in the range between picogram and milligram quantities and multiples and
3 dilutions thereof.

1 20. The method according to claim 1, wherein said predetermined curve is established
2 by correlating concentrations of at least one osteogenic factor with the probability of said
3 concentrations to generate bone *in vivo*.

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1 21. The method according to claim 20, wherein said correlating concentrations of at
2 least one osteogenic factor comprises correlating the product achieved by multiplying a
3 given concentration of TGF- β 1 with a concentration of BMP2, BMP4 or both.

1 22. The method according to claim 1 wherein said predetermined curve is established by
2 correlating concentration of at least one osteogenic factor with an ability to induce
3 differentiation of undifferentiated cells.

1 ~~23.~~ A method of measuring the osteogenic potential of an implant comprising:
2 (a) releasing osteogenic factors from said implant to produce an implant
3 releasate containing said osteogenic factors;
4 (b) quantifying the concentration of at least one osteogenic factor in said
5 implant releasate, wherein said quantifying occurs *in vitro* and does not require
6 implantation of said implant *in vivo* or use of complex biological living materials;
7 and
8 (c) determining a value of osteogenic potential for said implant by
9 corresponding said concentration of at least one osteogenic factor with a similar
10 value on a predetermined curve;
11 whereby the osteogenic potential of said implant is realized.

1 ~~24.~~ A method of measuring the chondrogenic capacity of an implant comprising:
2 (a) releasing chondrogenic factors from said implant to produce an implant
3 releasate containing said chondrogenic factors;
4 (b) quantifying the concentration of at least one chondrogenic factor in said
5 implant releasate, wherein said quantifying occurs *in vitro* and does not
6 require implantation of said implant *in vivo* or use of complex biological
7 living materials; and
8 (c) determining a value of chondrogenic capacity for said implant by
9 corresponding said concentration of at least one chondrogenic factor with a
10 similar value on a predetermined curve;
11 whereby the chondrogenic capacity of said implant is realized.

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1 ~~25.~~ A method of accelerating wound healing or the rate of recovery from bone
2 damage or disease in a human or non-human patient in need thereof comprising:

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- 4 (a) producing a composition comprising an amount of two or more growth
5 factors, wherein said amount effects enhanced healing over a composition
6 comprising just one of said two or more growth factors; and
7 (b) administering said composition to a patient in need thereof.

1 26. The method according to claim 25, wherein said amount is determined by
2 employing the method of claim 1.

1 ~~27.~~ A method for the diagnosis and treatment of bone or soft-tissue cancer in a human
2 or non-human patient in need thereof comprising:

- 3 (a) harvesting bone or soft-tissue from a donor;
4 (b) isolating and purifying osteogenic material therefrom; and
5 (c) comparing the quantity and type of growth factors present to that found
6 in healthy bone or other tissues.

1 ~~28.~~ A method for assessing developmental bone or tissue disorders comprising:
2 (a) harvesting a bone or soft-tissue sample from a selected area at different
3 stages of development;
4 (b) isolating, purifying and quantifying the osteogenic factors present in said
5 sample;
6 (c) comparing the quantity and type of osteogenic factors present at different
7 stages of the development of said bone or tissue with established baseline values;
8 and
9 (d) identifying osteogenic factors present in elevated or decreased concentrations
10 relative to said baseline value.

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1 29. The method according to claim 27, further comprising formulating therapeutic
2 compositions specific for counteracting said elevated or decreased concentrations of said
3 osteogenic factors.

1 30. The method of claim 27, wherein said elevated or decreased level is associated
2 with cellular proliferation, apoptosis, differentiation, morphogenesis or combinations
3 thereof.

31. A method for reducing the need to sacrifice laboratory animals used in bone growth studies comprising selecting an implant, wherein the osteoinductive potential of said implant is predetermined by the method of claim 1; and implanting said implant into a patient in need thereof.

32. An implant selected from a collection of like implants, wherein the osteoinductive potential of said collection of like implants is predetermined by the method of claim 1.

33. A collection of like implants, wherein the osteoinductive potential of said collection of like implants is quantified by the method of claim 1, and wherein said collection of like implants is labelled as possessing osteoinductive potential as determined by the method of claim 1.

1 ~~34.~~ A composition for administration to a site of need comprising an admixture of at
2 least one mitogenic factor and at least one morphogenic factor; wherein said composition
3 is adapted such that upon administration of said composition, an amount of said
4 morphogenic factor is released after an amount of said mitogenic factor is released.

1 35. The composition of claim 34, wherein said mitogenic factor is TGF-beta and said
2 morphogenic factor is BMP-2.

1 36. The composition of claim 34, wherein said admixture is provided in a
2 pharmaceutically acceptable carrier.